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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/915,873	07/26/2001	Anne-Marie Stomp	40989/237225(9280-12)	8799

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ALSTON & BIRD LLP
BANK OF AMERICA PLAZA
101 SOUTH TRYON STREET, SUITE 4000
CHARLOTTE, NC 28280-4000

EXAMINER
HELMER, GEORGIA L

ART UNIT	PAPER NUMBER
1638	10

DATE MAILED: 01/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/915,873	STOMP ET AL.	
	Examiner	Art Unit	
	Georgia L. Helmer	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *27-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,6,9* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Restriction election

1. The Office acknowledges the receipt of Applicant's restriction election, Paper No. 10, filed 12 November 2002. Applicant elects Group I, claims 1-26, with traverse. Applicant traverses, stating primarily that the search of Group I would encompass Groups II and III. Applicant's traversal has been considered and is unpersuasive because even if the searches may have some overlap, they are not coextensive. Therefore the restriction is proper.

2. Claims 1-34 are pending. Claims 27-34 are withdrawn as belonging to a non-elected invention.

3. Claims 1-26 are examined in the instant application. This restriction is made FINAL.

Information Disclosure Statement

4. An initialed and dated copy of Applicant's IDS forms 1449, Papers No. 4, 6, and 9, filed 16 January 2002, 24 April 2002, and 12 November 2002, respectively, is attached to the instant Office action.

Specification

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, see pages 8 and 12, for example. Applicant is

required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112-second

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-26 are rejected under 35 U.S.C. 112-2nd.

In claim 1 (b), "biologically active polypeptide" lacks antecedent basis. What does this term mean?

Claims 1 and 8 are incomplete methods because the desired product is not produced in the final step of the method.

Claim 2 properly belongs as a step in the process of claim 1. This step belongs between steps (a) and (b).

Claim 3, (c) "plant-preferred translation initiation context nucleotide sequence" is unclear. What does this mean? Where is this placed with respect to the other components of the nucleic acid construct?

Claim 9 (b), where are the recited elements positioned with respect to the other components of the nucleic acid construct?

In claim 14, "duckweed frond culture" lacks antecedent basis. What does "a biologically active multimeric protein" mean?

Claim 17 recites a "therapeutic" polypeptide. In what sense is the polypeptide therapeutic? To be therapeutic, the polypeptide must have a recited efficacy on something, or some defined condition.

Claim 18 recites biologically active polypeptides of a Markush group. What biological activity is intended for the various proteins?

In claim 19, "alpha-2b-interferon" needs an article in front of it.

In claim 20, " human alpha-2b-interferon" needs an article in front of it.

In claim 24, "signal peptide sequence" lacks antecedent basis.

All subsequent recitations of this language are also rejected.

Clarification and/or correction are required.

Claim Rejections - 35 USC § 112, first paragraph-Written Description

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 3-7, 9-13 and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 3-7 and 9-13 are drawn to nucleotide sequences that have duckweed-preferred codons in the coding sequence for a polypeptide, and to coding sequences comprising 70-100% Lemna-gibba or 70-100% Lemna-minor preferred codons. However, while the specification defines these as codons having a frequency of codon usage of at least 17%, the specification does not disclose which codons these are. Applicants are claiming a genus of sequences, yet there is no description of the structural features that define the genus.

See University of California v. Eli Lilly, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed, Cir. 1997), where it states: "The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA . . . Accordingly, the specification does not provide a written description of the invention . . ."

Claim 22 is drawn to a "biologically active variant" having 80% SEQ ID NO: to SEQ ID NO: 4 or 5. However, no structural element of the biologically active variant is recited. Applicants are claiming a genus of sequences, yet there is no description of the structural features that define the genus.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, one skilled in the art would not have been in possession of the genus claimed at the time this application was filed.

Claim Rejections - 35 USC § 112-Enablement

10. Claims 1-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The enablement issues are

- "duckweed-preferred codons" including Lemna gibba-preferred codons, and Lemna minor-preferred codons,
- "modified for enhanced expression",
- "human alpha-2b-interferon coding sequence", and
- "any biologically active variant".

Enablement is considered in view of the *Wands* factors (MPEP 2164.01(a)).

- *The nature of the invention, and the breadth of the claims.*

The claims are drawn to a method of producing a biologically active recombinant polypeptide in a duckweed culture, comprising culturing a duckweed stable transformed to express a biologically active recombinant polypeptide expressed from a nucleotide sequence for the polypeptide operatively liked to a coding sequence for a signal peptide that directs section of the polypeptide into the culture medium, and collecting biologically active polypeptide from the culture medium, where the nucleotide sequence has duckweed-preferred codons in the coding sequences, where the biologically active recombinant polypeptide is encoded by a nucleotide sequence that has been modified for enhanced expression in duckweed, wherein a multimeric protein is produced, where

the protein is collagen, hemoglobin, P450 oxidase, a monoclonal antibody, a mammalian polypeptide, a therapeutic polypeptide, where the mammalian polypeptide is insulin, growth hormone, alpha or beta interferon, beta glucocerebrosidase, beta-glycosidase, retinoblastoma protein, p53 protein, angiostatin, leptin, cytokines, receptors, human vaccines, animal vaccines, serum albumin, plant polypeptides, an alpha-2b-interferon, a human alpha-2b-interferon. Also to a signal peptide sequence of the human alpha-2b-interferon, the Arabidopsis thaliana chitinase signal peptide, the rice alpha amylase signal peptide, a duckweed signal peptide, a modified rice alpha amylase peptide, or a native signal peptide. And to stably transformed duckweed plant cultures.

- *The amount of guidance given, the presence of working examples and the predictability of the art.*

Re: "duckweed-preferred codons" including lemna-preferred codons:

Claims 3-7 are drawn to nucleotide sequences having "duckweed-preferred codons", or Lemna-preferred codons. Applicant describes (specification, p12) duckweed-preferred codons as referring to codons that have a frequency of codon usage of greater than 17%. Applicant cites that the percentages recited are obtained from the Codon Usage Database, and gives a Web address for this information; no hard copy of this information is provided in the specification. The use of this hyperlink does not provide enablement for the claimed invention because the material being cited is

material which maybe be changed at any time, and there is the possibility of constantly entering new matter into the specification. See MPEP 608.1.

Re: "modified for enhanced expression": Claims 8-13 are drawn to a nucleotide sequence "modified for enhanced expression in duckweed". Applicant recites this enhanced expression as resulting from the use of duckweed-preferred codons in the coding sequences (claim 9). However, the use of duckweed-preferred codons is not enabled, as discussed in the paragraph above. Applicant further recites a specific translation initiation codon and a plant intron. These further recited components may be present in the itemized list of DNA constructs used (Table 1, p 26) in the examples. However sufficient details are not given to demonstrate which, if any, of the claimed elements are present in the various constructs.

Re: " human alpha-2b-interferon coding sequence" and other sequences: The examples (Table 1, page 26) recite various sequences. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973). The examples

(Table 1, page 26) recite various sequences. Applicant claims a human alpha-2b-interferon coding sequence, but recites only a GeneBank Accession number for the sequence. Applicant claims a human alpha-2b-interferon signal peptide coding sequence, but recites only a GeneBank Accession number for the sequence. Applicant claims the *Arabidopsis thaliana* chitinase signal peptide sequence, but recites only a GeneBank Accession number for the sequence. To overcome these rejections, these sequence need to be submitted as a SEQ ID NO: and the SEQ ID NO: recited to enable these elements of the relevant constructs.

Re: a "biologically active variant" of an alpha-2b-interferon:

Applicant claims (claim 22) a "biologically active variant" of an alpha-2b-interferon, where the variant has at least 80% sequence identity with SEQ ID NO: 4 or SEQ ID NO: 5. Applicant recites various experimental data but does not enable any interferon sequences being expressed and having biological activity. Neither SEQ ID NO: 4 and 5, or any lesser sequence identity percentage of SEQ ID NO: 4 and 5 are taught to have the desired qualities. While working examples are not required, guidance must be given sufficient to enable one skilled in the art to make and use the claimed invention without undue experimentation. Applicant must provide sufficient guidance to address the issues of what comprises a "variant", whether any random sequences of the SEQ ID Nos can be altered, or what sequences and at what location, can be varied with impunity. Without such guidance, the experimentation required would not be routine, but would be undue.

In view of the breadth of the claims (a method of producing any biologically active recombinant polypeptide, any variant, any duckweed, any signal peptide, any biologically active polypeptide), the nature of the invention, the unpredictability of the art, the lack the lack of guidance in the specification, undue trial and error experimentations would be required to enable the invention as commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1, 2, 8, 15, 16, 17, 18, and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Stomp, et al, WO 99/07210, published 18 February 1999.

Stomp teaches a method of producing a biologically active recombinant polypeptide (p 9, lines 1-9) in a duckweed culture, where the nucleotide sequence comprising the coding sequence for the polypeptide is operably linked to a coding sequence for a signal peptide (p 12, lines 16-23) that directs secretion of the polypeptide into the culture medium (p 12, lines 16-23, and claim 49), and collecting the biologically active recombinant polypeptide from the culture medium (claim 49). Stomp also teaches producing a biologically active recombinant polypeptide where the polypeptide is encoded by nucleotide sequence that has been modified for enhanced

expression in duckweed (p 15, lines 18-28), a biologically active multimeric protein selected from the group of collagen, hemoglobin, P450 oxidase and a monoclonal antibody (p 9, lines 1-9), a mammalian polypeptide (p 9, lines 16-21), a therapeutic polypeptide (p 8, lines 2-5), a mammalian alpha interferon (p 8, lines 2-5), a biologically active recombinant polypeptide being an enzyme (p 8, lines 16-21).

Accordingly, Stomp anticipates the claimed invention.

Remarks

13. SEQ ID Nos 1, 3, 4, and 5 are taught in the prior art.

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Georgia L. Helmer whose telephone number is 703-308-7023. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 703-306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Georgia Helmer PhD
Patent Examiner
Art Group 1638
January 24, 2003

ELIZABETH F. McELWAIN
PRIMARY EXAMINER
GROUP 1600